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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Yuhpyng L. CHEN

Serial No.: 08/764110 Group Art Unit.1624

Filed: December 6, 1996 Examiner: BERCH, MARK L.

For: SUBSTITUTED HETEROCYCLIC DERIVATIVES

Attorney Docket No.: U 014197-9

RESPONSE UNDER 37 C.F.R. 1.116 EXPEDITED PROCEDURE EXAMINING GROUP

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SUBMISSION FOLLOWING FINAL REJECTION OF JUNE 27, 2001

This submission follows the advisory action of October 27, 2002 issued following the grant of the petition for revival of this application. A notice of Appeal was filed on August 19, 2003. This submission accompanies a request for continued examination of the application. Amendments to the claims are reflected in the listing of claims which is set out on page 2 hereof.

Remarks commence on page 11.

CERTIFICATE UNDER 37 CFR 1.10

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Amendments to the claims

This listing of the claims will replace all prior versions of the claims in this application.

Listing of Claims

Claim 1 (Cancelled).

Claim 2 (Previously amended) A compound according to claim 18 wherein R^1 is C_1- C_6 alkyl which may optionally be substituted with one hydroxy, fluoro, CF_3, or C_1-C_4 alkoxy group and may optionally contain one double or triple bond provided that at least two carbons are present in the C_1-C_6 alkyl group; and R^2 is benzyl, C_1-C_6 alkyl, which may optionally contain one double or triple bond provided that at least two carbons are present, where said C_1- C_6 alkyl and the phenyl moiety of said benzyl may optionally be substituted with one fluoro CF_3, or C_1-C_2 alkyl, C_1-C_2 alkoxy or chloro group.

Claim 3 (Previously amended) A compound according to claim 18 wherein: R^3 is methyl, ethyl, chloro or methoxy; R^4 is methyl, ethyl, or trifluoromethyl; G is hydrogen, methyl, ethyl, or E=G is C=O or C=S and R^5 is phenyl, pyridyl,, or pyrimidyl which is substituted with more than two substituents which are independently selected from C_1-C_4 alkyl and -O(C_1-C_4 alkyl), (C_1-C_4 alkyl)-O-(C_1 - C_2 alkyl), CF_3, OCF_3, -CHO, (C_1-C_4alkyl)-OH, CN, Cl, F, Br, I and NO_2, wherein one of the carbon-carbon single bonds of each of the foregoing (C_1-C_4)alkyl, groups having at least two carbons may optionally be replaced by a carbon-carbon double or triple bond.

Claim 4 (Previously amended) A compound according to claim 18 wherein A is N or A is CH or CCH_3 which may optionally be substituted by fluoro, chloro, CF_3, C_1-C_4 alkyl or C_1-C_4 alkoxy.

Claim 5 (Cancelled)

Claim 6 (Cancelled)

Claim 7 (Cancelled)

Claim 8 (Previously amended) A compound according to claim 18 wherein F is NR^4.

Claim 9 (Previously amended) A compound as claimed in claim 18 wherein F is CHR^4.

Claim 10 (previously amended) A compound according to claim 18 wherein F is nitrogen and is double bonded to E.

Claim 11 (Cancelled)

Claim 12 (Previously amended) A compound according to claim 18 wherein E is carbon.

Claim 13 (previously amended) A compound according to claim 18 wherein E is nitrogen.

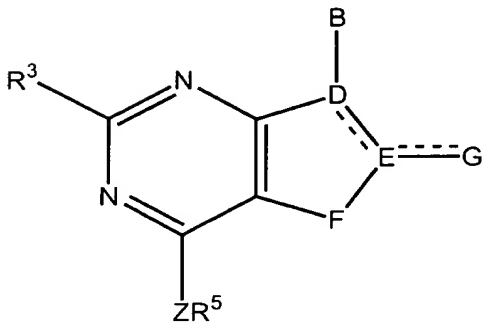
Claim 14 (Previously amended) A compound according to claim 18 wherein E is NR^{25} and R^{25} is hydrogen, C_1-C_4 alkyl or-CF_3,

Claim 15 (Cancelled)

Claim 16 (Cancelled)

Claim 17 (Cancelled)

Claim 18 (Presently amended). A compound of the formula



wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E, or D is CH and is single bonded to E;

F is CHR^4 or NR^4; provided that either 1) exactly one of D or E is nitrogen and F is CHR^4 or 2) F is NR^4 and neither D nor E is nitrogen ~~at least one of D and E is nitrogen or F is NR^4, and provided that only one of D and E is nitrogen and D and E are not nitrogen when F is NR^4~~;

G, when single bonded to E is hydrogen, C_1-C_4 alkyl, $-S(C_1$-C_4 alkyl), $-O(C_1$-C_4 alkyl), NH_2, $-NH(C_1$-C_4 alkyl) or $-N(C_1$-C_2 alkyl)(C_1-C_4 alkyl) wherein each of the C_1-C_4 alkyl groups of G may optionally be substituted by one hydroxy, $-O(C_1$-C_2 alkyl) or fluoro group; and G when double bonded to E is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D, is absent;

R^1 is hydrogen, C_1-C_6 alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1-C_4 alkoxy, CF_3, $-C(=O)O-(C_1$-$C_4)$alkyl, $-OC(=O)(C_1$-$C_4)$alkyl, $OC(=O)N(C_1$-C_4 alkyl)(C_1-C_2 alkyl), $-NHCO(C_1$-C_4 alkyl), $-COOH$, $-COO(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CON(C_1$-C_4 alkyl)(C_1-C_2 alkyl), $-S(C_1$-C_4 alkyl), $-CN$, NO_2, $-SO(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 alkyl), $-SO_2NH(C_1$-C_4 alkyl), $SO_2N(C_1$-C_4 alkyl)(C_1 - C_2 alkyl), wherein a carbon-carbon single bond of each of the C_1-C_4 alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-

carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1-C_4 alkyl groups in the foregoing R^1 groups having four carbon atoms may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1-C_{12} alkyl wherein one carbon-carbon single bond of any said alkyl group having at least two carbons, one or two carbon-carbon single bonds of any alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond; or R^2 is aryl or (C_1-C_4 alkylene)aryl, wherein said aryl and the aryl moiety of said (C_1-C_4 alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is C_3-C_8 cycloalkyl or (C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C_1-C_6 alkylene)(C_3-C_8 cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1-C_4 alkyl, or with one substitutent selected from bromo, iodo, C_1-C_6 alkoxy, -OC(=O)(C_1-C_6 alkyl), OC(=O)N (C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1 -C_6 alkyl), amino, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)-CO-(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl), -COOH, -COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), -SH, -CN, -NO_2, -SO(C_1-C_4 alkyl), -SO_2(C_1-C_4 alkyl), -SO_2NH(C_1-C_4 alkyl) and -SO_2N (C_1-C_4 alkyl)(C_1-C_2 alkyl);

-NR^1R^2 or -$CR^1R^2R^{10}$ may form a saturated 3 to 8 membered ring ~~consisting of single bonds wherein~~ which may optionally contain from 1 to 3 double bonds, that in the case where said ring is -$CR^1R^2R^{10}$ it is carbocyclic, subject to the proviso that when said ring ~~consisting of single bonds, wherein,~~ has from 5 to 8 members, one or two of the ring carbon atoms of such a 5 to 8 membered ring may optionally and independently br replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, ~~and wherein from one to three of the single bonds of such a 3 to 8 membered ring that are carbon-carbon or carbon-nitrogen single bonds may each optionally be replaced by a double bond~~;

R^3 is hydrogen, C_1-C_4 alkyl, O(C_1-C_4 alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C_1-C_4 alkyl) or -SO_2(C_1-C_4 alkyl) wherein each of the (C_1-C_4 alkyl) moieties in the foregoing R^3

groups may optionally be substitued with one substituent R^9 selected from hydroxy, fluoro and (C_1-C_2 alkoxy);

each of R^4 is, independently hydrogen, (C_1-C_6 alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, -O(C_1-C_4 alkyl), N (C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), -SO_2(C_1-C_4 alkyl), -CO(C_1-C_4 alkyl), -C(=O)H or C(=O)O (C_1-C_4 alkyl), wherein one or two of the carbon-carbon single bonds in each of the (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties in the foregoing R^4 groups may optionally be replaced with a carbon-carbon double or triple bond and wherein each of said (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties may optionally be substitued with one or two substituents independently selected from hydroxy, amino, C_1-C_3 alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH_3, fluoro, chloro, ~~C_1-C_3 alkylthio~~, -CN, -COOH, -C(=O)O(C_1-C_4 alkyl), -C(=O)(C_1-C_4 alkyl) and NO_2;

R^5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C_3-C_8 cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^4 wherein N^4 is hydrogen, C_1-C_4 is alkyl or benzyl; and wherein each of the foregoing R^5 groups is substituted with from one to four substituents wherein one to three of said substituents may be selected, independently, from chloro, C_1-C_6 alkyl and -O(C_1-C_6 alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF_3, -NO_2, -NH_2, -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_6 alkyl), -C(=O)O(C_1-C_4 alkyl), -C(=O)(C_1-C_4 alkyl), -COOH, -SO_2NH(C_1-C_4 alkyl), -SO_2N (C_1-C_2 alkyl) (C_1-C_4 alkyl), -SO_2NH_2, $NHSO_2$(C_1-C_4 alkyl),-S(C_1-C_6 alkyl) and -SO_2(C_1-C_6 alkyl), and wherein each of the C_1-C_4 alkyl and C_1-C_6 alkyl, moieties in the foregoing R^5 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl; and furthermore wherein when R^5 is phenyl or pyridyl substituted with three substituents, said substituents can further be selected from (C_1-C_4 alkyl)O(C_1-C_4 alkyl), OCF_3, and fluoro, and one carbon-carbon single bond of each (C_1-C_4) alkyl group of said substituents having between two and four carbon atoms may be optionally replaced with a carbon-carbon double or triple bond; or R^5 is pyrimidyl substituted by three substituents independently selected from C_1-C_4 alkyl, -O(C_1-C_4 alkyl), CF_3, OCF_3, -CHO, (C_1-C_4 alkyl)-OH, CN, Cl, F, Br, I and NO_2, wherein a carbon-carbon single bond of said (C_1-C_4) alkyl groups

having been two and four carbon atoms may optionally be replaced by a carbon-carbon double or triple bond;

R^7 is hydrogen, C_1-C_4 alkyl, halo, cyano, hydroxy, -O(C_1-C_4 alkyl) -C(=O)(C_1-C_4 alkyl), -C(=O)O(C_1-C_4 alkyl), -OCF_3, -CF_3, -CH_2-OH, -CH_2O(C_1-C_4 alkyl);

R^{10} is hydrogen, hydroxy, methoxy or fluoro;

R^{11} is hydrogen or C_1-C_4 alkyl; and

with the proviso that: (a) when R^4 is attached to nitrogen, it not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

Z is NH, oxygen, sulfur, -N(C_1-C_4 alkyl), -NC(=O)(C_1-C_2 alkyl) NC(-O)O(C_1-C_2 alkyl or CR^{13} R^{14} wherein R^{13} and R^{14} are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R^{13} and R^{14} can be cyano;

or a pharmaceutically acceptable salt of such compound.

Claim 19 (Cancelled)

Claim 20 (Cancelled)

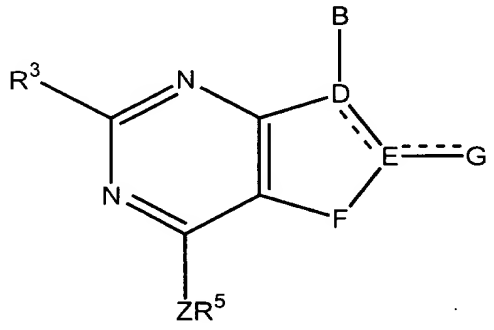
Claim 21 (Cancelled)

Claim 22 (Cancelled)

Claim 23 (Cancelled)

Claim 24 (Cancelled)

Claim 25 (Presently amended) A compound of the formula



wherein the dashed lines represent optional double bonds;

B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$;

E is nitrogen, CH or carbon;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E, or D is CH and is single bonded to E;

F is CHR^4 or NR^4; provided that **either 1) exactly one of D or E is nitrogen and F is CHR^4 or 2) F is NR^4 and neither D nor E is nitrogen** ~~at least one of D and E is nitrogen or F is NR^4, and provided that only one of D and E is nitrogen and D and E are not nitrogen when F is NR^4~~];

G, when single bonded to E is hydrogen, C_1-C_4 alkyl, $-S(C_1$-C_4 alkyl), $-O(C_1$-C_4 alkyl), NH_2, $-NH(C_1$-C_4 alkyl) or $-N(C_1$-C_2 alkyl)(C_1-C_4 alkyl) wherein each of the C_1-C_4 alkyl groups of G may optionally be substituted by one hydroxy, $-O(C_1$-C_2 alkyl) or fluoro group; and G when double bonded to E is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D, is absent;

R^1 is hydrogen, C_1-C_6 alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C_1-C_4 alkoxy, CF_3, $-C(=O)O-(C_1$-$C_4)$alkyl, $-OC(=O)(C_1$-$C_4)$alkyl, $OC(=O)N(C_1$-C_4 alkyl)(C_1-C_2 alkyl), $-NHCO(C_1$-C_4 alkyl), -COOH, $-COO(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CON(C_1$-C_4 alkyl)(C_1-C_2 alkyl), $-S(C_1$-C_4 alkyl), -CN, NO_2, $-SO(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 alkyl), $-SO_2NH(C_1$-C_4 alkyl), $SO_2N(C_1$-C_4 alkyl)(C_1 - C_2 alkyl), wherein a carbon-carbon single bond of each of the C_1-C_4 alkyl groups in the foregoing R^1 groups having at least two carbons may optionally be replaced with a carbon-carbon double or triple bond, and one or two carbon-carbon single bonds of each of the C_1-C_4 alkyl groups in the foregoing R^1 groups having four carbon atoms may optionally be replaced with a carbon-carbon double or triple bond; R^2 is C_1-C_{12} alkyl wherein one carbon-carbon single bond of any said alkyl group having at least two carbons, one or two carbon-carbon single bonds of any alkyl having at least four carbons, and from one to three carbon-carbon single bonds of any said alkyl having at least six carbons may optionally be replaced with a carbon-carbon double or triple bond; or R^2 is aryl or (C_1-C_4 alkylene)aryl, wherein said aryl and the aryl moiety of said (C_1-C_4 alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl,

pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; or R^2 is C_3-C_8 cycloalkyl or (C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C_1-C_6 alkylene)(C_3-C_8 cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1-C_4 alkyl, or with one substitutent selected from bromo, iodo, C_1-C_6 alkoxy, -OC(=O)(C_1-C_6 alkyl), OC(=O)N (C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1 -C_6 alkyl), amino, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)-CO-(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl), -COOH, -COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), -SH, -CN, -NO_2, -SO(C_1-C_4 alkyl), -SO_2(C_1-C_4 alkyl), -SO_2NH(C_1-C_4 alkyl) and -SO_2N (C_1-C_4 alkyl)(C_1-C_2 alkyl);

-NR^1R^2 or -$CR^1R^2R^{10}$ may form a saturated 3 to 8 membered ring ~~consisting of single bonds wherein~~ which may optionally contain from 1 to 3 double bonds, that in the case where said ring is -$CR^1R^2R^{10}$ it is carbocyclic, subject to the proviso that when said ring ~~consisting of single bonds, wherein,~~ has from 5 to 8 members, one or two of the ring carbon atoms of such a 5 to 8 membered ring may optionally and independently br replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1-C_4 alkyl, benzyl and C_1-C_4 alkanoyl, ~~and wherein from one to three of the single bonds of such a 3 to 8 membered ring that are carbon-carbon or carbon-nitrogen single bonds may each optionally be replaced by a double bond~~;

R^3 is hydrogen, C_1-C_4 alkyl, O(C_1-C_4 alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C_1-C_4 alkyl) or -SO_2(C_1-C_4 alkyl) wherein each of the (C_1-C_4 alkyl) moieties in the foregoing R^3 groups may optionally be substitued with one substituent R^9 selected from hydroxy, fluoro and (C_1-C_2 alkoxy);

each of R^4 is, independently hydrogen, (C_1-C_6 alkyl), fluoro, chloro, bromo, iodo, trifluoromethyl, hydroxy, cyano, amino, nitro, -O(C_1-C_4 alkyl), N (C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), -SO_2(C_1-C_4 alkyl), -CO(C_1-C_4 alkyl), -C(=O)H or C(=O)O (C_1-C_4 alkyl), wherein one or two of the carbon-carbon single bonds in each of the (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties in the foregoing R^4 groups may optionally be replaced with a carbon-

carbon double or triple bond and wherein each of said (C_1-C_6 alkyl) and (C_1-C_4 alkyl) moieties may optionally be substitued with one or two substituents independently selected from hydroxy, amino, C_1-C_3 alkoxy, dimethylamino, methylamino, ethylamino, -NHC(=O)CH_3, fluoro, chloro, ~~C_1-C_3 alkylthio~~,-CN, -COOH, -C(=O)O(C_1-C_4 alkyl), -C(=O)(C_1-C_4 alkyl) and NO_2;

R^5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C_3-C_8 cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^4 wherein N^4 is hydrogen, C_1-C_4 is alkyl or benzyl; and wherein each of the foregoing R^5 groups is substituted with from one to four substituents wherein one to three of said substituents may be selected, independently, from chloro, C_1-C_6 alkyl and -O(C_1-C_6 alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF_3, -NO_2, -NH_2, -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_6 alkyl), -C(=O)O(C_1-C_4 alkyl), -C(=O)(C_1-C_4 alkyl), -COOH, -SO_2NH(C_1-C_4 alkyl), -SO_2N (C_1-C_2 alkyl) (C_1-C_4 alkyl), -SO_2NH_2, $NHSO_2$(C_1-C_4 alkyl),-S(C_1-C_6 alkyl) and -SO_2(C_1-C_6 alkyl), and wherein each of the C_1-C_4 alkyl and C_1-C_6 alkyl, moieties in the foregoing R^5 groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R^7 is hydrogen, C_1-C_4 alkyl, halo, cyano, hydroxy, -O(C_1-C_4 alkyl) -C(=O)(C_1-C_4 alkyl), -C(=O)O(C_1-C_4 alkyl), -OCF_3, -CF_3, -CH_2-OH, -CH_2O(C_1-C_4 alkyl);

R^{10} is hydrogen, hydroxy, methoxy or fluoro;

R^{11} is hydrogen or C_1-C_4 alkyl; and

with the proviso that: (a) when R^4 is attached to nitrogen, it not halo, cyano or nitro; and (b) one of E, D and F must be nitrogen or substituted nitrogen, and only one of E, D and F can be nitrogen or substituted nitrogen;

Z is NH, oxygen, sulfur, -N(C_1-C_4 alkyl), -NC(=O)(C_1-C_2 alkyl) NC(-O)O(C_1-C_2 alkyl or CR^{13} R^{14} wherein R^{13} and R^{14} are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R^{13} and R^{14} can be cyano;

or a pharmaceutically acceptable salt of such compound.

REMARKS

Claims 18 and 25 have been amended to meet most of the points raised in the final rejection and the issues noted in the advisory action. In particular,

1) the definition of the $CR^1R^2R^3$ has been amended. So far as the first issue raised in the advisory action having regard to the ring (presumably intended to refer to a $CR^1R^2R^{10}$ ring) is concerned, the original disclosure at page 4 states that $CR^1R^2R^{10}$ may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from 1 to 3 double bonds and wherein 1 or 2 of the ring carbon atoms of such 5 to 8 membered rings may optionally be independently replaced by oxygen sulfur or NZ^3. There is an obvious inconsistency in this definition having regard to whether certain rings need to be 3 to 8 membered or 5 to 8 membered. The wording now adopted is the most limited possible interpretation of this original language and avoids the possibility that the group could be an azetidine as postulated by the Examiner by permitting replacement of ring carbon atoms by nitrogen only in the situation where the ring contains from 5 to 8 members.

2) The "alkylthio" language has been deleted.

3) The examiner's proposed wording for the provisoes in the definition of F has, except for an obvious typographical error, been adopted in both of claims 18 and 25.

It is, however, respectfully submitted that the definition of R^4 as CF_3 should be acceptable. The original definition in claim 1 included C_1-C_6 alkyl ... optionally substituted with one or two substituents independently selected from ... fluorine.... . Page 9 refers to R^4 as trifluoromethyl but only in juxtaposition to other groups having certain particular definitions. The applicants have previously argued that each of these groups of definitions should be taken separately. The examiner argues that they are cumulative. The Examiner has not so far been persuaded. However, there is an obvious discrepancy between two parts of the original disclosure which requires a sensible resolution. On page 9, it is indicated that the more specific

embodiments of the invention include compounds wherein R^4 is trifluoromethyl. To read this consistently with the definition in original claim 1 and on page 4, means that R^4 as trifluoromethyl must fall within the broad definition given in these locations, otherwise it could not be a more specific embodiment. The sensible resolution of this discrepancy therefore, is to add trifluoromethyl to the definition of R^4 in the claims and on page 4. The Examiner's emphasis on the semicolon at page 9, line 10, seems misplaced. Semicolons when used in a list can mean either "or" or "and", depending upon the context. Normally, this can be determined by the conjunction used between the penultimate and ultimate members of the list. Unfortunately, in the present case, no conjunction was used. However, it is submitted that the natural reading of the second complete paragraph on page 9 is that this is listing preferred groups which may be selected independently of each other.

In view of the foregoing it is believed that this application is now in order for allowance. An early action to this end is respectfully solicited. If the Examiner believes it would be useful to discuss this matter either personally or in a telephone interview, he is requested to let us know so that this can be arranged.

Respectfully submitted,

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Registration No. 31053

OIPE JC10 NOV 21 2003 PATENT & TRADEMARK OFFICE

Practitioner's Docket No. U-014197-9 ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Yuhpyng L. CHEN
Application No.: 08/764,110 Group No.: 1624
Filed: DECEMBER 6, 1996 Examiner: BERCH, MARK L.
For: SUBSTITUTED HETEROCYCLIC DERIVATIVES

Mail Stop RCE
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION (RCE) (37 C.F.R. 1.114)

1. Applicant hereby requests continued examination, in accordance with 37 C.F.R. Section 1.114, for the above identified application.

CERTIFICATION UNDER 37 C.F.R. SECTIONS 1.8(a) AND 1.10
*(When using Express Mail, the Express Mail label number is **mandatory**; Express Mail certification is optional.)*

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

37 C.F.R. Section 1.8(a)

X with sufficient postage as first class mail.

37 C.F.R. Section 1.10

☐ as "Express Mail Post Office to Addressee" Mailing Label No. _____ **(mandatory)**

TRANSMISSION

☐ facsimile transmitted to the Patent and Trademark Office (703) _____

Date: November 19, 2003

_____
Signature

JOHN RICHARDS
(type or print name of person certifying)

• Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.

11/25/2003 SLUANG1 00000010 08764110
01 FC:1801 770.00 OP
02 FC:1251 110.00 OP

NOTE: ***37 C.F.R. § 1.114 Request for continued examination:***

"(a) If prosecution in an application is closed, an applicant may request continued examination of the application by filing a submission and the fee set forth in § 1.17(e) prior to the earliest of:

(1 Payment of the issue fee, unless a petition under § 1.313 is granted;

(2) Abandonment of the application; or

(3) The filing of a notice of appeal to the U.S. Court of Appeals for the Federal Circuit under 35 U.S.C. 141, or the commencement of a civil action under 35 U.S.C. 145 or 146, unless the appeal or civil action is terminated.

(b) Prosecution in an application is closed as used in this section mans that the application is under appeal, or that the last Office action is a final action (§ 1.113), a notice of allowance (§ 1.311), or an action that otherwise closes prosecution in the application.

(c) A submission as used in this section includes, but is not limited to, an information disclosure statement, an amendment to the written description, claims, or drawings, new arguments, or new evidence in support of patentability. If reply to an Office action under 35 U.S.C. 132 is outstanding, the submission must meet the reply requirements of § 1.111.

(d) If an applicant timely files a submission and fee set forth in § 1.17(e), the Office will withdraw the finality of any Office action and the submission will br entered and considered. If an applicant files a request for continued examination under this section after appeal, but prior to a decision on the appeal, it will be treated as a request to withdraw the appeal and to reopen prosecution f the application before the examiner. An appeal brief under § 1.192 or a reply brief under § 1.193(b), or related papers, will not be considered a submission under this section."

NOTE: An applicant may file a submission under 37 C.F.R. 1.114 containing only an information disclosure statement (37 C.F.R. 1.97 and 1.98) in an application subject to a notice of allowance under 35 U.S.C. § 151. An appeal brief or a reply brief (or related papers) will not be considered a submission under 37 C.F.R. 1.114. See 37 C.F.R. 1.114(d). The submission, however, may consist of the arguments in a previously filed appeal brief or reply brief, or may simply consist of a statement that incorporates by reference the arguments in a previously filed appeal brief or reply brief. In addition, a previously filed amendment after final may satisfy this submission requirement. American inventor's Protection act of 1999, Question & Answer A5.

NOTE: Even though an RCE is improper (e.g., because it was filed before the prosecution is closed), an amendment submitted with the RCE will still be entered and considered by the examiner since it was timely filed and responsive to the non-final Office action in compliance with 37 C.F.R. 1.111. American Inventor's Protection Act of 1999, Question & Answer A4.

WARNING: *35 U.S.C. 132(b) and Section 1.114 provide for the continued examination of an application and* ***not*** *examination of a continuing application). Accordingly, the Office will not permit an applicant to obtain continued examination on the basis of claims that are independent and distinct from the claims previously claimed and examined. Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.*

WARNING: *The provisions of 37 C.F.R. 1.114 also do not apply (1) to a provisional application; (2) an application for a utility or plant patent filed under 35 U.S.C. 111(a) before June 8, 1995; (3)) an international application filed under 35 U.S.C. 363 before June 8, 1995 (4) a patent under reexamination or (5) an application for a design patent. 37 C.F.R. § 1.114(e).*

WARNING: The PTO has pointed out why § 1.97(b) does not provide that an information disclosure statement will be considered it is filed within three months after the date of a request for continued examination under § 1.114. The PTO explained that since an RCE filing is a reply under 35 U.S.C. 132, the applicant may be entitled to patent term adjustment if the Office does not act on an application containing a request for continued examination under § 1.114 within four months. See 35 U.S.C. 154(b)(1)(A)(ii). Thus, the Office cannot delay action on RCE applications for three months to determine whether an information disclosure statement will be filed. The Office, however, is adopting provisions (§ 1.103(c)) for a limited suspension of action after the filing of a request for continued examination under § 1.114, for the applicant to obtain additional time (prior to the issuance of the next Office action) to provide an information disclosure statement (or amendments, or an affidavit or declaration) after the filing of the RCE. See Notice of August 16, 2000, "Request for Continued Examination Practice and Changes to Provisional Application Practice; Final Rule", 65 Fed. Reg., pages 50091-50105, at page 50100 (comment 11); OG: September 5, 2000, pages 13-24.

WARNING: *One of the time periods excluded from patent term adjustment is the time consumed by a continued examination request under 35 U.S.C. 132(b) (§ 1.114(b)(1)).*

WARNING: *The Office will not suspend action in an application when a reply by the applicant is outstanding. 35 U.S.C. 133 requires an applicant to "prosecute the application" within six months of an Office action (or a shorter period as set in the Office action) to avoid abandonment of the application. If an applicant files a request for continued examination but does not also provide any submission (in reply to the prior Office action) within the period for reply to the prior Office action, the application is abandoned by operation of law (35 U.S.C. 133).*

The Office will treat a request for continued examination under § 1.114 containing a bona fide submission that is not fully responsive to the prior Office action under the practice set forth in § 1.135(c). In addition, under the limited suspension of action provisions of § 1.103(c), an applicant must still file a request for continued examination practice in compliance with § 1.114, but may obtain additional time (prior to the issuance of the next Office action) to provide an information disclosure statement, amendments, or an affidavit or declaration after the filing of the request for continued examination.

See Notice of August 16, 2000. "Request for Continued Examination Practice and Changes to Provisional Application Practice; Final Rule", 65 Fed. Reg., pages 50091-50105, at page 50102 (comment 20); OG: September 5, 29000, ages 13-24, Page 50102.

WARNING: *Section 197(b) does not provide that an information disclosure statement will be considered if it is filed within three months after the date of request for continued examination under § 1.114.*

NOTE: *There is no limit to the number of times the fee for continued examination may be submitted. Notice of March 10, 2000, 65 Fed. Reg. 14865. at 14868.*

NOTE: *Unlike a continuation application, a continued examination request* ***can*** *utilize the mailing procedure of 37 C.F.R. 1.8. See 37 C.F.R. Section 1.8(a)(2)(i)(A).*

TIME REQUEST IS BEING MADE

2. This request is being submitted *(check appropriate item(s) below)*:

i. [X] Prior to abandonment of the application

ii. [X] Payment of the issue fee
- [X] Prior to payment of issue fee
- [ ] Issue fee has been paid but a petition under Section 1.313 has been granted

iii. [X] Prior to a decision on appeal to the Board of Patent Appeals & Interferences
- [ ] A notice is being separately sent to the Board of Patent Appeals & Interferences that this Request for Continued Examination is being filed.

NOTE: *If such a notice is not sent to the Board, they may refuse to vacate a decision rendered after the filing of the RCE but before recognition by the Office of the RCE request under Section 1.114.*

iv. [X] Appeal to the U.S. Court of Appeals of the Federal Circuit under 35 U.S.C. 145 or Commencement of a civil action under 35 U.S.C. 146
- [X] Prior to the filing of such appeal or commencement of civil action
- [ ] Such appeal or commencement of civil action has been terminated

ENCLOSURES

3. Do not automatically enter any prior unentered amendment(s). Herewith **as the required submission** is/are:

[ ] Request hereby to enter unetered amendment(s) of _____.

[ ] An information disclosure (37 C.F.R. Section 1.98)
[ ] Form PTO-1449 (PTO/SB/08A and 08B)

[X] An amendment

[ ] New arguments

[ ] New evidence in support of patentability

WARNING: *If reply to a final or non-final Office action under 35 U.S.C. 132 is outstanding, the submission must meet the reply requirements of Section 1.111. 37 C.F.R. Section 1.114(b).*

[ ] Other:

FEE FOR REQUEST (37 C.F.R. Section 1.17(e)).

4. This application is on behalf of:

[ ]	Small entity (and status is still as small entity)	$ 385.00
[X]	Other than a small entity	$ 770.00
	Continued Prosecution Request Fee	$ 770.00

FEE FOR CLAIMS

NOTE: *"The fee for continued examination under Section 1.114 (Section 1.17(e)) does not include additional claims fee (cf. 1.53 (d)(3)(ii))." See Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.*

37 C.F.R. 1.53(d)(3) : "The filing fee for a continued prosecution application filed under this paragraph is:

(i) The basic filing fee as set forth in Section 1.16; and

(ii) Any additional Section 1.16 fee due based on the number of claims remaining in the application after entry of any amendment accompanying the request for an application under this paragraph and entry of any amendments under Section 1.116 unentered in the prior application which applicant has requested to be entered in the continued prosecution application."

5. The fee for claims (37 C.F.R. Section 1.16(b)-(d)) has been calculated as shown below:

	(Col.1)		(Col. 2)	(Col. 3)	SMALL ENTITY			OTHER THAN A SMALL ENTITY	
	Claims Remaining After Amendment		Highest No. Previously Paid For	Present Extra	Rate	Addit. Fee	*OR*	Rate	Addit. Fee
Total	9	Minus	20	=	x $9 =	$		x $18 =	$ 0
Indep.	2	Minus	3	=	x $43 =	$		x $86 =	$0
[ ] First Presentation of Multiple Dependent Claim					+ $145 =	$		+ $290 =	$
					Total Addit. Fee	$___	*OR*	**Total Addit. Fee**	$0___

* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3,
** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest No. Previously Paid For" (Total or Indep.) is the highest number found in the appropriate box in Col. 1 of a prior amendment or the number of claims originally filed.

WARNING: *See 37 C.F.R. Section 1.116.*

EXTENSION OF TIME

(If an extension of time is appropriate complete (a) or (b), as applicable)

6. The proceedings herein are for a patent application, and the provisions of 37 C.F.R. Section 1.136(a) apply.

(a) [X] Applicant petitions for an extension of time, the fees for which are set out in 37 C.F.R. Section 1.17(a)(1)-(4), for the total number of months checked below:

Extension for (months)	Fee for other than small entity	Fee for small entity
[X] one month	$ 110.00	$ 55.00
[ ] two months	$ 420.00	$ 210.00
[ ] three months	$ 950.00	$ 475.00
[ ] four months	$1,480.00	$ 740.00
	Fee	$110.00

If an additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

[ ] An extension for _____ months has already been secured, and the fee paid therefor of $ _____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request $ 110.00

OR

(b) [ ] Applicant believes that no extension of time is required. However, this is a conditional petition and authorization to pay the necessary fees to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

TOTAL FEE(S) DUE

WARNING: *The fee for continued examination under Section 1.114 may not be deferred. 37 C.F.R. Section 1.53(f).*

7. The total fee(s) due is/are:

Continued Prosecution Fee (Section 1.17(e))	$ 770.00
Fee(s) for additional claims (if any) (Section 1.16(b)-(d))	$ _____
Extension of time fee (if any) (Section 1.17(a)(1)-(4))	$ 110.00
Total Fee(s) Due:	$ 880.00

PAYMENT OF FEE(S) DUE

8. Please pay the fee(s) for this continued examination application as follows:

[2] Checks are attached for the sum of $ 880.00

[ ] Charge Account _____ the sum of $ _____

Please charge any required additional fee(s) for Section 1.17(e), Section 1.16(b)-(d) and/or Section 1.17(a)(1)-(4) or refund overpayment to

[x] Deposit Account 12-0425

INVENTORSHIP

NOTE: Any change of inventors must be via the procedure set forth in 37 C.F.R. Section 1.48. See Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.

9. This application as amended names as inventors:

[X] the same inventors as previously designated for the claims.

[ ] fewer than the inventors previously designated and a statement accompanies this request for the deletion of the name or names of the person or persons who are not inventors of the invention now being claimed.

[ ] a person not named previously as an inventor and a petition under 37 C.F.R. Section 1.48 is/has separately:
[ ] being filed
[ ] been filed

DEFERRAL OF EXAMINATION

10. [ ] A request for deferral of examination accompanies this request for continued examination.

SIGNATURE OF PRACTITIONER

Reg. No.:

JOHN RICHARDS
(type or print name of practitioner)

Tel. No.: ( )

P.O. Address

Customer No.:

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